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Registration Decision RD2013-07

Kasugamycin

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Publications
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6604-E2
Ottawa, Ontario K1A 0K9

Internet: pmra.publications@hc-sc.gc.ca
healthcanada.gc.ca/pmra
Facsimile: 613-736-3758
Information Service:
1-800-267-6315 or 613-736-3799
pmra.infoserv@hc-sc.gc.ca

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Registration Decision for Kasugamycin

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting full registration for the sale and use of Kasugamycin Technical Bactericide and Kasumin 2L Bactericide, containing the technical grade active ingredient kasugamycin, to control or suppress bacterial diseases on greenhouse and field fruiting vegetables, pome fruits and walnuts.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

These products were first proposed for registration in the consultation document[1] Proposed Registration Decision PRD2012-30, *Kasugamycin*. This Registration Decision[2] describes this stage of the PMRA's regulatory process for kasugamycin and summarizes the Agency's decision and the reasons for it. The PMRA received no comments on PRD2012-30. This decision is consistent with the proposed registration decision stated in PRD2012-30.

For more details on the information presented in this Registration Decision, please refer to the Proposed Registration Decision PRD2012-30, *Kasugamycin* that contains a detailed evaluation of the information submitted in support of this registration.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[3] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions of registration. The Act also requires that products have value[4] when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

3 "Acceptable risks" as defined by subsection 2(2) of *Pest Control Products Act*.

4 "Value" as defined by subsection 2(1) of *Pest Control Products Act*"...the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact".

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

What Is Kasugamycin?

Kasugamycin is an aminoglycoside antibiotic that is produced by *Streptomyces kasagiensis*, which was first isolated from a soil sample collected in Nara, Japan. It prevents protein synthesis in bacterial cells.

Health Considerations

Can Approved Uses of Kasugamycin Affect Human Health?

Kasumin 2L Bactericide containing kasugamycin is unlikely to affect your health when used according to label directions.

Potential exposure to kasugamycin may occur through the diet (food and water) or when handling and applying the end-use product Kasumin 2L Bactericide. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when pesticide-containing products are used according to label directions.

In laboratory animals, Kasugamycin Technical Bactericide was of low acute toxicity via the oral, dermal and inhalation routes of exposure. It was moderately irritating to the eyes; therefore, the signal word and hazard statement "WARNING – EYE IRRITANT" are required on the label. It was minimally irritating to the skin. The potential for an allergic reaction was identified and the hazard statement "POTENTIAL SENSITIZER" is required on the label.

The acute toxicity of the end-use product Kasumin 2L Bactericide was low via the oral, dermal and inhalation routes of exposure. It was minimally irritating to the skin and eyes. The potential

for an allergic reaction was identified and the hazard statement "POTENTIAL SENSITIZER" is required on the label.

Kasugamycin did not cause cancer in animals and did not damage genetic material. There was no indication of damage to the nervous or immune systems. Health effects in animals given repeated doses included effects on the skin at points of contact, kidneys, testes and blood. Kasugamycin did not cause birth defects in animals; however, reduced fertility was noted in males at high doses.

When kasugamycin was given to pregnant animals, minor effects on the skeleton of the developing fetus were observed at doses that were toxic to the mother, indicating that the young do not appear to be more sensitive to kasugamycin than the adult animal.

The risk assessment protects against the effects of Kasugamycin Technical Bactericide by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Residues in Water and Food

Dietary risks from food and water are not of concern

Aggregate dietary intake estimates (food plus water) revealed that the general population and infants, the subpopulation which would ingest the most kasugamycin relative to body weight, are expected to be exposed to less than 3.0% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from kasugamycin is not of concern for all population sub-groups.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit. Pesticide maximum residue limits are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Food containing a pesticide residue that does not exceed the established residue limit does not pose an unacceptable health risk.

Residue trials conducted throughout Canada and the United States using kasugamycin on fruiting vegetables (CG 8-09), pome fruits (CG 11-09) and walnuts were acceptable. The maximum residue limit for this active ingredient can be found in the Science Evaluation section of the consultation document.

Risks in Residential and Other Non-Occupational Environments

Exposures of adults, youths and children, through contact with transferable residues following commercial application of kasugamycin to residential fruit trees and pick-your-own orchards, are not of concern.

The risk to individuals through contact with transferable residues following commercial application of kasugamycin on residential fruit trees (for example, apples, pears) was assessed and determined not to be of concern.

Taking into consideration label requirements that include the timing of applications and the long pre-harvest interval, the risk to adults, youth and children that enter treated orchards for "pick-your-own" activities is not of concern.

Occupational Risks From Handling Kasumin 2L Bactericide

Occupational risks are not of concern when Kasumin 2L Bactericide is used according to the proposed label directions, which include protective measures.

Farmers and custom applicators who mix, load or apply Kasumin 2L Bactericide as well as field workers re-entering treated fields, nurseries and greenhouses can come in direct contact with Kasumin 2L Bactericide residues on the skin. Therefore, the label specifies that anyone mixing/loading and applying Kasumin 2L Bactericide, and during clean-up and repair, must wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes. The label also requires that workers do not enter treated fields, orchards, and greenhouses for 12 hours after application. Taking into consideration these label statements, the number of applications and the expectation of the exposure period for handlers and workers, the risks to these individuals are not a concern.

For bystanders, exposure is expected to be much less than that for workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When Kasugamycin Is Introduced Into the Environment?

Kasugamycin is not expected to persist in the environment and is not expected to pose a risk to wild mammals, birds, earthworms, honeybees, or aquatic organisms. A risk to terrestrial plants was identified; therefore, statements on the product label are required to inform users of the potential risks, and no-spray buffer zones (2 meters) are required during application to protect habitats downwind of the application site.

Kasugamycin enters the environment when used as a bactericide on the foliage of pome fruit trees, walnut trees and field-grown fruiting vegetables (also proposed for greenhouse fruiting vegetables). Kasumin 2L Bactericide is applied by field sprayer or airblast application and, as such, there is a potential that non-target terrestrial and aquatic habitats may be exposed to the chemical as a result of spray drift or runoff.

Once in the environment, kasugamycin is broken down by microbial activity in soil and in water/sediment systems and is expected to be slightly to moderately persistent in the environment. Kasugamycin is not volatile and is not expected to be detectable in air. Leaching to

groundwater is not expected to be a concern for either the parent compound or the transformation products. Kasugamycin is highly soluble in water and is likely to move off the treated field and enter aquatic environments. Two major transformation products, kasugamycinic acid and kasugabiosamine, are produced in water and are not expected to persist in the environment. Hydrolysis may be an important process in the transformation of kasugamycin (particularly at higher pH), while phototransformation is not considered an important route of transformation on soil or in water. In aquatic environments kasugamycin is not likely to accumulate in fish tissues.

Kasugamycin is not expected to pose risks to wild mammals, birds, earthworms, honeybees and aquatic organisms at the proposed use rates. A risk to terrestrial plants was identified; thus, to minimize the potential for exposure resulting from off-field drift, no-spray buffer zones will be required between the treated area and downwind terrestrial habitats. No environmental risk is expected from potential exposure to the major transformation products of kasugamycin.

Value Considerations

What Is the Value of Kasumin 2L Bactericide?

Kasumin 2L Bactericide is an antibiotic that controls or suppresses bacterial diseases on greenhouse and field fruiting vegetables, pome fruits and walnuts. It controls fire blight on pome fruits. Kasumin 2L Bactericide represents a valuable tool for management of bacterial diseases given the limited number of registered alternatives available as well as the resistance issues and limitations stemming from the use of streptomycin and copper.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the label of Kasumin 2L Bactericide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Because there is a concern with users coming into direct contact with Kasumin 2L Bactericide on the skin or through inhalation of spray mists, anyone mixing, loading and applying Kasumin 2L Bactericide must wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes. The label also requires that workers not enter treated fields, orchards, and greenhouses for 12 hours after application. In addition, standard label statements to protect against drift during application were added to the label.

Environment

No-spray buffer zones of two meters are required for the protection of non-target terrestrial habitats.

Additional advisory statements on the potential for runoff of kasugamycin residues to adjacent aquatic habitats are required.

Other Information

The relevant test data on which the decision is based (as referenced in PRD2012-30, *Kasugamycin* are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

Any person may file a notice of objection[5] regarding this registration decision within 60 days from the date of publication of this Registration Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides and Pest Management portion of the Health Canada's website (Request a Reconsideration of Decision, www.hc-sc.gc.ca/cps-spc/pest/part/protect-proteger/publi-regist/index-eng.php#rrd) or contact the PMRA's Pest Management Information Service.

[5] As per subsection 35(1) of the *Pest Control Products Act*.